

## REMARKS

Claims 29, 31-32, and 35-48 are pending.

### **I. METHOD CLAIMS 36-38 AND 46-48 FOR NEAR INFRARED IN VIVO FLUORESCENCE IMAGING**

#### Claim Rejections Under 35 U.S.C. §103

These claims stand rejected as allegedly being obvious over Ohno in view of U.S. Pat. No. 6,258,340 (Licha I) in further view of US Pat. No. 6,083,485 (Licha II) and U.S. Pat. No. 6,114,350 (Randall). Applicants respectfully traverse these rejections. Licha I and II may hereinafter be collectively referred to as "Licha," since one is a continuation of the other.

First, Ohno is certainly non-analogous art because it is not from the same field of endeavor as the present invention (near IR fluorescence imaging) and is not reasonably pertinent to the problem which the inventor is involved. See *In re Clay*, 966 F.2d 656, 23 U.S.P.Q. 2d 1058 (Fed. Cir. 1992). Ohno pertains to photosensitive materials having a hydrophilic colloid layer containing a photochemically inert dye (column 1, lines 10-16) for use in photographic emulsions. This has nothing to do with the methods of the captioned claims. Moreover, the PTO has not even alleged that Ohno relates to any problem that the inventors were concerned with. Photographic emulsions have nothing to do with in vivo near IR fluorescence imaging and relevant problems, e.g., contrast agents having solubility in water, safety in a living body, capability of distinguishing normal tissues from diseased tissues, etc. See present specification at paragraph bridging pages 2-3. As a result, this reference is highly non-analogous art and cannot be used in an obviousness rejection of the method claims. As such, the Action has failed to establish a *prima facie* obvious case. (Even if Ohno were relevant, including its specific K<sup>+</sup> compounds, it cannot render use of the claimed Na<sup>+</sup> compounds obvious. There are so many structural variations possible from column 3 of Ohno, as discussed below, that nothing motivates a skilled worker to modify by only replacing K<sup>+</sup> by Na<sup>+</sup>. *In re Jones*, 958 F.2d 347, 21 U.S.P.Q. 1941 (Fed. Cir. 1992). See below.)

Moreover, Licha and Randall provide generic formulas encompassing vast numbers of compounds, essentially infinite in scope. See Formula IIa at columns 17 and 18 of Licha I, Formula IIa at columns 5-6 of Licha II, and Formula 2 at columns 6-8 of Randall. However, these references in no way render the claimed invention obvious alone or even if combined, as alleged. Note Licha's

disclosure that its vast numbers of substances “may have quite different properties.” See, e.g. Licha I at column 13, lines 35 – 41 and Licha II at column 14, lines 28 – 33. Particularly, there are no blazemarks or guideposts whatsoever, e.g. preferences or examples or any other aspects, to lead one of skill in the art to the sodium salts of the claimed invention from the extremely broad generic teachings.

Licha and Randall fail to provide any blazemarks to a compound having three or more sulfonic acid groups in a molecule or to an L<sup>4</sup> methine as required in all claims substituted by alkyl (or S-alkyl) having 1 to 4 carbon atoms or alkyl (or S-alkyl) having 1 to 4 carbon atoms and substituted by a sulfonic acid group. Rather, Licha and Randall strongly teach away by exemplifying compounds having fewer sulfonic acid groups and no such methine substitution at the 4 position. See examples at columns 13 – 17 of Licha I, at columns 14 – 18 of Licha II, and Randall at columns 9 - 17.

This case is governed by *In re Baird*, 29 USPQ2d 1550 (Fed. Cir. 1994), where a disclosure of vast numbers of compounds did not render obvious a claim to a subclass of its encompassed subject matter. The reference in Baird rendered obvious a narrower class of molecules which was actually taught, i.e., those having structures as in the preferences and examples. The prior art’s disclosure thus indicated preferences leading away from the claimed compounds. The situation here is the same. Licha and Randall, alone or in combination, cannot render *prima facie* obvious the claimed invention.

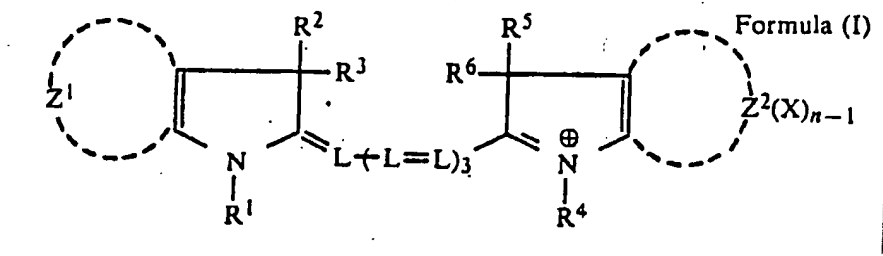
## **II. COMPOUND CLAIMS**

### **Claim Rejections Under 35 U.S.C. §102**

Claims 29, 31-32, 35, and 39-45 stand rejected as allegedly being anticipated by U.S. Pat. No. 4,839,265 (Ohno). Applicants respectfully traverse these rejections.

First, Applicants traverse the assertion that the compound (I-7) at columns 5 – 6, which is a potassium salt, is within the scope of the instant claims.

Second, with respect to the partial passage cited at column 3, lines 20-25, nothing leads one of skill in the art specifically to only this part of the passage. Applicants respectfully submit that the action is inaccurate by failing to recite the whole passage, which is:



wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ , and  $R^6$  are the same or different, each represents substituted or unsubstituted alkyl groups; and each of  $Z^1$  and  $Z^2$  represents a group of non-metallic atoms necessary for the formation of a substituted or unsubstituted benzo-condensed ring or naphtho-condensed ring; provided that among the groups  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $Z^1$ , and  $Z^2$  at least 3 groups, and preferably 4 to 6 groups, have an acid substituent group (e.g., sulfonic group and carboxylic group) respectively, and preferably they permit the dye molecule to have 4 to 6 sulfonic groups. In this specification, the sulfonic group represents a sulfo group and a salt thereof, and the carboxylic group represents a carboxyl group and a salt thereof. Examples of the salt include alkali metal salts (e.g., Na and K), ammonium salts, and organic ammonium salts (e.g., triethylamine, tributylamine, and pyridine).

$L$  represents a substituted or unsubstituted methine group; and  $X$  represents an anion. Examples of the anion represented by  $X$  include halogen ions (such as Cl and Br), p-toluenesulfonic acid ion, and ethyl sulfate ion.

$n$  represents 1 or 2; and it is 1 when the dye forms an inner salt.

See column 3, lines 1-33.

For an anticipation rejection to be proper, the reference must clearly and unequivocally disclose or direct those skilled in the art to the claimed compound without any need for picking, choosing, and combining various disclosures in the teachings of the cited reference. *See, e.g., In re Arkley et al.*, 172 U.S.P.Q. 524 (CCPA 1972).

Nothing in Ohno leads a skilled worker to the claimed subject matter. The example cited by the Examiner (I-13, column 7-8 of Ohno) is a potassium salt, one of thirty compounds disclosed at columns 3 – 12. At column 3, at least 20 variables are disclosed and defined in Formula I. An anticipation rejection is not proper if picking and choosing is required. Nothing in Ohno would lead

one, even if selecting compound I-13, to choose specifically only a salt variation of example 13 from among the very many modifications possible from column 3. There is no preference to pick just the salt cation for modifying out of the many other variables. On this basis alone, there is no anticipation.

But even if one did choose to vary the salt using impermissible hindsight, nothing leads one to select the Na<sup>+</sup> salts recited in the instant claims from among the many other salts, e.g. alkali metal salts, ammonium salts, and organic ammonium salts, disclosed. In this regard, the Federal Circuit has held that a reference must clearly and unequivocally disclose the claimed compounds or direct those skilled in the art to make the particular selection necessary to arrive at the claimed subject matter. *See, supra, In re Arkley*. Rather, the Action uses improper hindsight picking and choosing to assert the anticipation rejection. *See, also, In re Rushig*, 145 U.S.P.Q. 274 (CCPA 1965). Consequently, the rejections should be withdrawn.

#### Nonobviousness

All these claims are nonobvious for essentially the same reasons as discussed above. Ohno is simply not part of the analogous art and nothing in the other references alone or in combination leads one to the claimed invention.

Moreover, the present invention exhibits significant and unexpected results, as discussed in Applicants' last reply. Particularly, the examiner apparently relies on example I-13 (column 8) of Ohno as the closest prior art species. (See also column 6, compound I-5.) As the examiner notes, such compounds have 4 carbon atoms in the alkyl chain connected to the N-atoms of the molecules. These compounds also differ in degree of sulfonation, 4 or 5, respectively. In the comparative data, compounds 31 and 43 have two or four, respectively, carbon atoms in the same position and also have different degrees of sulfonation. As the data show, the sodium salts of compounds 31 and 43, in each case, have unexpected and significant superiority in LD<sub>50</sub> values compared to the corresponding potassium salts. See page 84, last two lines, of the specification. Ohno discloses only the potassium salts of its closest prior art compounds, not the sodium salts.

Regarding the Examiner's comments on these data at the top of page 5 of the Office Action, the data are not demonstrating property differences due to degrees of sulfonation. Rather, they demonstrate property differences based on Na and K.

Consequently, Applicants respectfully submit that the rejections should be withdrawn.

As noted on page 5 of the amendment filed on April 18, 2003, applicants have filed a certified copy of JP 10/283301. See also the attached copy of the PTO date-stamped filing receipt.

Claim Rejections Under 35 U.S.C. §112, second paragraph

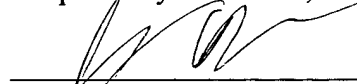
Claims 41-43 stand rejected as allegedly being indefinite. Applicants respectfully traverse these rejections.

The Action alleges that because the base claims can have sulfonic groups at various positions, claiming a specific number of sulphonic groups renders the claims indefinite. Applicants respectfully submit that the claims are sufficient to apprise one of ordinary skill in the art of their scopes. All reasonable possibilities are included in the claims. Therefore, the claims serve the notice function required by 35 U.S.C. §112, second paragraph. There is no ambiguity. This notice is all that is required to meet the requirements of 35 U.S.C. §112. See, e.g., *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1379, 55 USPQ2d 1279, 1283 (Fed. Cir. 2000) and M.P.E.P. §2173.02. Thus, Applicants respectfully submit that these rejections should be withdrawn.

In view of the above remarks, favorable reconsideration is courteously requested.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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